Remarks

Favorable consideration of this application is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-12 and 14-20 are pending in the application. Claims 1-12 and 14-20 have been rejected. Claims 1, 12, 15, and 16 have been amended, support for which can be found within the present application. No new matter has been added.

Claim Objections

The Examiner alleges that "this application contains claims drawn to an invention nonelected without traverse in the paper filed on October 21, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action." Applicants note that no mention of this was made in the last Office Action (January 12, 2006), which was filed by the Office in response to Applicants' restriction requirement response. In the course of electing Group I (claims 1-12 and 14-20) on October 21, 2005, Applicants withdrew claims and 13 and 21-23, marking them as such in subsequent filings.

A rereading of the Restriction Requirement of October 5, 2005 reveals that the Examiner called claims 12 and 15 generic, and accordingly requested the naming of a single species of a mutant isoform, and a cell line, respectively, within those claims. For that reason, Applicants have amended claims 12 and 15 accordingly, thereby obviating the claim objection. No new matter has been added.

Rejection Under 35 USC §112, Second Paragraph

Claims 16 remains rejected under 35 U.S.C. §112, second paragraph, as being indefinite, and expresses confusion over whether the "endogenous promoter" of the claim is present in the knock-in construct or is present in the genome of the cell. The "endogenous promoter" of the claim is meant to apply to the genome of the cell, and claim 16 has been amended accordingly.

Rejection Under 35 USC §112, First Paragraph- Written Description

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner states the following:

> [t]he instant claims broadly encompass a method of expressing a specific isoform of any gene product, in any cell (claim 20), or any mammalian cell (claim 1), absent other isoforms of said gene product, comprising introducing into said cell a ds RNA having at least 95% sequence identity to a common nucleic acid sequence shared by two or more isoforms of said gene product. As such, the claims require knowledge of numerous

desired isoforms of a gene product, whether endogenous to said cell or isoforms that may be exogenous in origin. Knowledge of numerous isoforms would also be required to determine the nature of the sequences that would constitute a common and shared nucleic acid.

In addition to the arguments advanced in the last Office Action response (and while not acknowledging their insufficiency), Applicants hereby respectfully disagree with the Examiner, and request the withdrawal of the present rejection for at least the following reasons:

I. The Present Application Provides Adequate Written Description Support for the Elements and Steps of the Present Method Claims

Applicants continue to contend that (i) they need not provide written description support for *every gene product*, and (ii) that Example 18 of the USPTO's "Revised Interim Written Description Guidelines Training Materials" (which can be found at http://www.uspto.gov/web/offices/pac/writtendesc.pdf) is still apposite to the present claims.

Applicants recognize the point made by the Examiner at the bottom of page 4 of the present Office Action, that "method claims encompassing a claimed genus of nucleic acid isoforms still require an adequate written description of said genus." Applicants also recognize that Example 18 of the Written Description Guidelines, which involved gene expression in *Neurospora crassa*, finds written description support present because "there is no substantial variation within the genus." Applicants disagree with the Examiner's contention, however, that the genus of the present claims is so substantial that the logic of Example 18 does not apply.

That there is a wide variety of gene products encoded by the nucleic acids of the present claims is not in dispute. However, the gene products themselves (e.g., the encoded proteins) of the claimed nucleic acids, are not essential to the claimed invention. The functional, biological, or structural properties, of the gene products encoded nucleic acids of the claims does not at all impact the presently claimed methods. Whether the gene product of the claimed nucleic acids is a GPCR, or enzyme, or a structural protein, is- in the words of Example 18- not essential to the claimed invention.

For this reason, there is no substantial variation within the genus- i.e., practitioners of the claimed invention are interested in the nucleic acids of the present claims only in terms of the presence and number of their isoforms, and the nucleic acid sequences thereof, and not in terms of the gene products encoded thereby. The members of the claimed genus must all have two or more isoforms which are capable of being knocked down by using RNA inhibition, and the only variation between said members is in terms of their nucleic acid sequence (and how the isoform of interest of a gene product differs sequence-wise from the other isoforms).

Another statement from Example 18 of the Written Description Guidelines applies to the present claims: "The art indicates that there is no substantial variation within the genus because there are a limited number of ways to practice the process steps of the claimed invention." Indeed, the steps of the claimed methods are similarly applied to all nucleic acids with one or more isoforms, irrespective of the gene products encoded thereby.

II. Practitioner of the Present Method Claims Only Requires Knowledge Related to Her Gene Product of Interest

Applicants reiterate that, for a variety of reasons, the present claims do not require knowledge of every possible isoform of every gene product that is capable of expression via multiple isoforms. As stated in the last Office Action response, Applicants averred that "a practitioner of the present method claims only requires knowledge *related to her gene product of interest*." So as to avoid an argument of semantics with the Examiner, Applicants wish to change the statement to "a practitioner of the present method claims only need possess knowledge relating to her gene product of interest."

The meaning of the statements is the same, but Applicants fear the Examiner took the "only requires..." to mean that a practitioner of the present invention would have to actively seek knowledge about her gene product of interest (i.e., would not be equipped with), in order to practice the present invention. Such is not the case, and Applicants argue that one would already possess information about her gene product of interest before employing the presently claimed methods. In fact, one would not even be interested in the presently claimed methods if she did not already (i) know about the isoforms of her gene product of interest; (ii) wish to isolate one of them in particular. Therefore, Applicants contend that the Examiner's following statement is inapposite to the present invention (from page 5 of the Office Action): "In response, it is noted that while a particular practitioner would require knowledge related to her gene product of interest, such knowledge is in fact absent from the instant specification..."

III. Applicants are not Required to Explicitly List in the Patent Specification Every Isoform for A Gene Product of Interest

According to §2163.07(a) of the MPEP, Applicants need not list things explicitly in the patent specification which are inherently disclosed instead. Applicants respectfully contend that the principles of §2163.07(a) are at work here, in that Applicants do not have to explicitly show all isoforms of a gene product of interest because they are inherent in the present invention (whether endogenous in the target cell or introduced by expression vector).

Rejection Under 35 USC §112, First Paragraph- Enablement

Claims 1-12 and 14-20 are rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide an enablement for the full scope of the invention. Applicants respectfully disagree for at least the following reasons:

Although Applicants mention *supra* that a practitioner of the presently claimed methods will already possess information about the isoforms of her gene product of interest, it is worth pointing out that Applicants described in great detail in the last Office Action response (of July 12, 2006) the ease with which a practitioner of ordinary skill in the art can find publicly-available information about the isoforms of a given gene product of interest. The Examiner mentioned on page 5 of the present Office Action the unsuitability of this line of reasoning for a response to a written description rejection ("Further, Applicants arguments regarding additional experimentation are pertinent to issues of enablement, and not written description.") However, the Examiner never addressed the same with respect to the Enablement rejection, stating instead, "The response to Applicants arguments regarding the requirement to characterize the isoforms to a gene product of interest... has been addressed supra." Applicants therefore remain without an explanation as to the Examiner's perception of insufficiency of the Applicants' reasoning along these lines with respect to the Enablement rejection, and respectfully request one.

Furthermore and importantly, the Applicants have amended claim 1 (and all dependent claims therefrom) to include only in vitro methods. Applicants have therefore obviated the major aspects of the present enablement rejection, including that the present claims formerly read on gene therapy, that the delivery of RNAi *in vivo* is problematic, and that the administration of expression vectors was not sufficiently explained in the specification. Without acquiescing to the Examiner's rejection, Applicants have nevertheless obviated it by their present amendment of claim 1.

For at least the reasons stated above, Applicants respectfully request withdrawal of the enablement rejection of claims 1-12 and 14-20.

Rejection Under 35 USC §102(e)

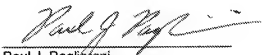
Claims 1-12 and 14-20 are rejected under 35 U.S.C. §102(e), as anticipated by Tuschl et al. (U.S. Patent Publn. No.: 2004/0259247)(hereafter, "the Tuschl reference"). The Examiner was not persuaded by the Applicants' reasoning in the last response, and therefore, the rejection from the last Office Action (dated January 12, 2006) is maintained.

While Applicants remain convinced of their reasoning and argumentation in their July 12, 2006 response, they present herewith a declaration pursuant to 37 C.F.R. § 131, swearing behind the Tuschl reference, thereby obviating the rejection.

The 131 declaration is attested to and signed by inventor Malgorzata Anna Kisielow, and furnishes evidence of a date of invention prior to the filing date of the Tuschl reference (i.e., prior to the 102(e) date of November 29, 2001). For this reason, Applicants respectfully submit that the 102(e) rejection in view of the Tuschl reference be removed.

Applicants respectfully request entry of the amendments to the claims and the specification and submit no new matter is added thereby. Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,



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